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DFT studies of imino and thiocarbonyl ligands with the pentaaqua Mg²⁺ cation: affinity and associated parameters

Leonardo Moreira da Costa · Glaucio Braga Ferreira · José Walkimar de M. Carneiro

Abstract The affinity of the pentaaqua Mg^{2+} cation for a set of *para*-substituted imino [$HN=CHC_6H_4(R)$] and thiocarbonyl [$S=CHC_6H_4(R)$] ligands (R=H, F, Cl, Br, OH, OCH_3, CH_3, CN, NH_2 and NO_2) was analyzed with DFT (B3LYP/6-31+G(d)) and semi-empirical (PM6-DH2) methods. The interaction enthalpy was calculated to quantify the affinity of the Mg^{2+} cation for the ligands. Additionally, geometric and electronic parameters were correlated with the intensity of the metal-ligand interaction. The imino ligands have stronger interaction with the pentaaqua Mg^{2+} cation than the thiocarbonyl derivatives. The electronic nature of the substituent is the main parameter that determines the interaction enthalpy. Ligands with electron donor substituents have more exothermic interaction enthalpies than those with electron withdrawing groups. The HSBA analysis showed that the interaction between the Mg^{2+} cation and hard bases (imino ligands) is stronger than with soft bases (thiocarbonyl derivatives). The EDA analysis showed that the electrostatic, covalent and repulsion components of the interaction are the most affected by the substituent, whereas the dispersion and exchange components are almost constant.

L. M. da Costa · G. B. Ferreira · J. W. de M. Carneiro
Programa de Pós-Graduação em Química,
Universidade Federal Fluminense, Niterói, Brazil

G. B. Ferreira · J. W. de M. Carneiro (✉)
Departamento de Química Inorgânica,
Instituto de Química, Universidade Federal Fluminense,
Outeiro de São João Batista, s/n,
24020-141 Niterói, RJ, Brazil
e-mail: walk@vm.uff.br

Introduction

The interaction between metal aquacomplexes and neutral bases is a subject of continuous interest in biochemistry, as the majority of biological reactions occur in the water media [1, 2]. The Mg^{2+} cation is the fourth most abundant cellular ion [3] involved in a wide range of biological processes that contributes to the homeostasis of organisms [4]. This cation is an essential cofactor for many enzymes [5], being vital for the structural organization of the DNA and RNA chains [6], metabolism of fats and proteins, permeability of the cell membrane, neuromuscular excitability and the modulation of the vascular tone of arteries [4, 7]. In all these processes the Mg^{2+} cation interacts with a diverse variety of biological ligands with several different functional groups. The most common types of interactions are with oxygen atoms of alcohols [8], carboxylic acids [9] and phosphates [10], nitrogen atoms of amines [11], amides [12] and imines [13] and sulfur atoms of thiols [14]. In the biological media the Mg^{2+} cation is usually surrounded by different types of atoms [4] forming interactions with a high electrostatic component due to its small size and high effective nuclear charge [15]. Several works report that in the biological media the Mg^{2+} cation is preferentially surrounded by hard bases [16–18].

Computational studies have extensively contributed to the understanding of the interaction between metal cations and ligands. Yanez et al. have published a set of papers showing that the strength of the metal-ligand interaction is mainly

affected by the metal oxidation state, specific electron densities, orbital energy distribution and steric effects of the ligands [19–23]. A detailed DFT study of the influence of electron donor and electron acceptor groups on the metal affinity in a series of *para*-substituted pyridine complexes was reported by Palusiak [24]. It has been shown that pendant aromatic groups can modulate the strength of the metal-ligand interaction, which is correlated with geometric and electronic parameters of the ligand. This behavior was also found by Senapati et al. [25], and Gal et al. [26] in complexes with *para*-substituted phenyl rings. Ma has shown that the interaction between metal cations with O-, N- and S-containing ligands is predominantly electrostatic, although the covalent contribution seems to be important to the final interaction energy and geometry [27]. Bayat et al. reported an energy decomposition study [28] for interaction of divalent cations with oxime ligands showing that complexes with electron donor substituents have the strongest metal-ligand interaction energies and that neighboring groups directly modulates the strength of the electrostatic term of the interaction. Similar trends were found in other studies [29–31].

Continuing our previous investigations [32–35] about the effect of substituents on the interaction between metal cations and neutral ligands, in the present work we quantify the intensity of binding of *para*-substituted imino [HN=CHC$_6$H$_4$(R)] and thiocarbonyl [S=CHC$_6$H$_4$(R)] ligands to the Mg^{2+} cation. The ligands are schematically shown in Fig. 1. *Para*-substituted groups (R=NH$_2$, OCH$_3$, OH, CH$_3$, H, F, Cl, Br, CN and NO$_2$) with different inductive and resonance properties [36] were chosen to simulate the electronic modulation on the cation affinity. Based on experimental and theoretical studies [37–40] on the coordination number of Mg^{2+} in aqueous media, we considered the Mg^{2+} cation coordinated to six water molecules in an octahedral arrangement and determined the energy for substitution of one of these water molecules by a monofunctional, thiocarbonyl and imino, ligand, as shown in Fig. 1. Additionally, geometric and electronic parameters of the systems as well as the electrostatic, covalent and repulsive components of the metal ligand interaction were evaluated and correlated with the substitution energy. We have also calculated the global softness index of each monofunctional ligand to predict the binding preference to the Mg^{2+} cation through the theory of hard and soft acids and bases (HSAB) [41–43]. Over the course of the past few decades, this theory has proven to be a useful tool for the prediction of the affinity of ligands for metal centers [44–47].

Computational details

Geometry optimizations and energy calculations were carried out with the Gaussian 09 software [48], using the B3LYP functional [49] with the 6-31+G(d) basis set [50]. After geometry optimization the second order force constant matrix
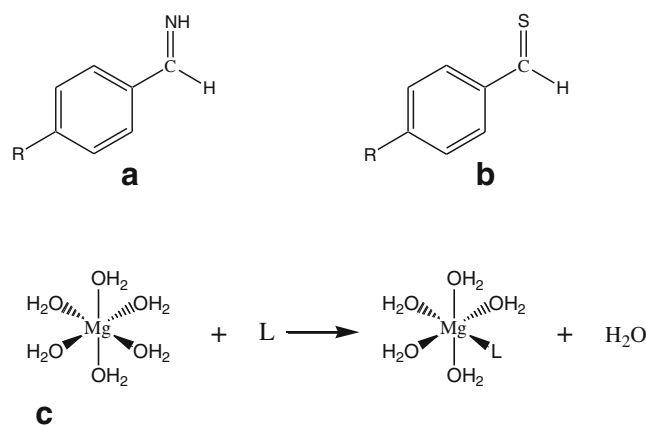

Fig. 1 Structure of the imino (**a**) and thiocarbonyl (**b**) ligands used for the pentaaqua Mg^{2+} complexation (R=H, F, Cl, Br, OH, OCH$_3$, CH$_3$, CN, NH$_2$ and NO$_2$) and (**c**) general scheme for the substitution of a water molecule from the [Mg(H$_2$O)$_6$]$^{2+}$ aquacation for one monofunctional ligand

was calculated to confirm the optimized geometry as a genuine minimum on the potential energy surface. It has been shown that these combinations of methods and basis set are able to yield structures in reasonable agreement with those obtained at higher level of theory [16, 32–35]. To evaluate the ability of a less time consuming method to reproduce the magnesium cation affinity, semi-empirical PM6 [51] calculations were also carried out with the MOPAC 2009 package [52]. EDA calculations [53] were done using the B3LYP functional and the 6-31+G(d) basis set [48] of the GAMESS software [54, 55]. The HSBA analysis was performed with the B3LYP/6-31+G(d) method. The quantification of the absolute softness is based on the HSAB theory and may be calculated according to Eq. 1 [41–43]:

$$S = 1/[(E_{anion} - E_{neutral}) - (E_{neutral} - E_{cation})], \qquad (1)$$

where E$_{anion}$, E$_{neutral}$ and E$_{cation}$ are the ground state energies of the ligand as a monoanionic, neutral and as a monocationic species, respectively.

Results and discussion

Geometry optimization The geometries of the 20 substituted pentaaqua magnesium complexes were fully optimized with the DFT and semi-empirical methods in an arrangement as shown in Fig. 2. The geometries of the complexes in each set of ligands are similar, with the exception of the d$_1$ (distance between metal and coordinating ligand atom) and d$_2$ (bond length of the double bond, C=N or C=S, for imino and thiocarbonyl derivatives, respectively) distances that are more strongly affected by the electronic effects of the *para*-substituted groups.
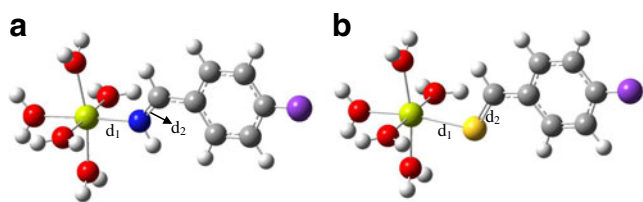
Fig. 2 General scheme for the optimized structures of the imino (**a**) and thiocarbonyl (**b**) complexes. The d_1 and d_2 distances are the bond lengths between the Mg^{2+} cation and the ligand (N or S atoms) and the ligand double bond, respectively

In Table 1 we list the d_1 distances for the imino and thiocarbonyl complexes. As the interaction between alkaline earth cations and neutral ligands has a strong electrostatic component [15], the distance between the Mg^{2+} cation and the nitrogen/sulfur atom (highest charged atoms) of the ligand must be an indicator of its strength. Table 1 shows that the imino complexes have smaller d_1 distances than the corresponding thiocarbonyl compounds, thus indicating that the electrostatic component of the interaction must be stronger for the imino derivatives. The d_1 distances in the imino complexes are 0.447 ± 0.008 Å smaller than for the thiocarbonyl complexes, due to the larger van der Waals radius of the sulfur atom and the higher charge concentration on the nitrogen atom of the imino derivatives [27,

32–35]. The d_1 distances in each set of ligands are smaller for electron donor substituents than for compounds with electron withdrawing groups, indicating that the electronic nature of the substituent is related to the strength of the interaction. The correlation between geometrical trends and the nature of the substituent was previously reported in a set of studies [24–26, 32–35]. The resonance effect of the *para*-substituted group of the ligand modulates the negative charge on the atom (S or N) that interacts with the metal cation, directly affecting the strength of the electrostatic component of the interaction and changing the d_1 distance according to this modulation. For the d_1 distance the difference between the stronger electron donor (NH_2) and the stronger electron acceptor (NO_2) groups is 0.040 Å for the imino complexes and 0.068 Å for the thiocarbonyl compounds. The last value is higher probably due to the softer and more easily polarizable electronic cloud of the thiocarbonyl derivatives.

In Table 1 we also show the variation in the d_2 distance (Δd_2) as a consequence of complexation. The d_2 bond length depends mainly on the atomic radii of the atoms that participate in the bond and are not directly related to the strength of the metal-ligand interaction, although the variation of its double bond character may be correlated with the interaction energy. Analysis of resonance structures of the derivatives shows that complexes with electron donor groups dislocate

Table 1 Absolute softness of the ligand (**S**), interatomic metal-ligand (**d_1**) distance, variation in the ligand double bond distance due to complexation (Δd_2) in Å, B3LYP and PM6 interaction enthalpies (ΔH and E_{PM6}) and B3LYP interaction Gibbs free energy (ΔG^{298}) in kcal mol^{-1}, mulliken atomic charges on the atom (N or S) that interacts with the pentaaqua Mg^{2+} cation (**qX**) and on the whole ligand (**qL**) in $|e^-|$ for the imino and thiocarbonyl ligands

R	S	d_1	Δd_2	ΔH	E_{PM6}	ΔG^{298}	qX	qL
Imino ligands								
NH_2	3.223	2.095	0.035	−30.51	−44.59	−30.12	−0.671	0.196
OCH_3	3.207	2.104	0.033	−26.05	−39.09	−25.30	−0.575	0.188
OH	3.189	2.109	0.031	−23.29	−35.12	−22.57	−0.570	0.184
CH_3	3.180	2.114	0.028	−22.11	−33.72	−23.29	−0.560	0.175
H	3.169	2.122	0.026	−19.39	−32.72	−18.64	−0.558	0.166
F	3.148	2.125	0.024	−16.41	−29.36	−15.72	−0.553	0.161
Cl	3.139	2.125	0.024	−16.71	−29.66	−16.07	−0.554	0.162
Br	3.136	2.123	0.025	−17.62	−29.89	−16.98	−0.555	0.163
CN	3.110	2.130	0.020	−9.40	−24.27	−8.83	−0.547	0.155
NO_2	3.013	2.135	0.018	−7.25	−19.27	−6.84	−0.423	0.147
Thiocarbonyl ligands								
NH_2	4.128	2.529	0.059	−24.09	−38.45	−24.06	−0.221	0.348
OCH_3	3.995	2.543	0.056	−18.77	−33.03	−18.71	−0.200	0.336
OH	3.889	2.549	0.055	−15.59	−30.78	−15.26	−0.194	0.329
CH_3	3.882	2.560	0.051	−13.97	−28.15	−13.24	−0.180	0.326
H	3.875	2.568	0.049	−9.92	−24.96	−9.61	−0.168	0.322
F	3.862	2.575	0.047	−7.92	−23.45	−7.60	−0.164	0.318
Cl	3.855	2.574	0.047	−8.49	−23.87	−8.22	−0.165	0.318
Br	3.852	2.572	0.048	−9.73	−24.56	−9.28	−0.166	0.319
CN	3.849	2.587	0.046	−0.84	−19.24	−0.69	−0.139	0.308
NO_2	3.838	2.597	0.042	1.93	−15.83	1.73	−0.121	0.302

electron density from the double bond to the N or S atoms strengthening the interaction and reducing the double bond character. The d_2 distance increases due to complexation for either the electron donor or the electron withdrawing groups. However, this effect is more pronounced in the electron donor derivatives. In this way, Table 1 shows that complexes with electron donor groups have higher Δd_2 values than those with electron withdrawing groups, in agreement with previous studies [32–35]. The Δd_2 difference between the amino and nitro derivatives is 0.017 Å for both the imino and the thiocarbonyl complexes, indicating that the variation of the Δd_2 distance is not determined by the atoms forming the double bond, but only by the electronic nature of the substituent.

Interaction enthalpy The affinity of the imino and thiocarbonyl ligands for the pentaaqua Mg^{2+} cation was evaluated in terms of the interaction enthalpy, obtained as the heat of reaction of Eq. 2, corrected to 298 K with the thermal contribution using unscaled frequencies. The same methodology has been previously used to determinate the affinity of ligands for metal cations [16–18, 24–27, 32–35].

$$\left[Mg(H_2O)_6\right]^{2+} + L \rightarrow \left[Mg(H_2O)_5L\right]^{2+} + H_2O \qquad (2)$$
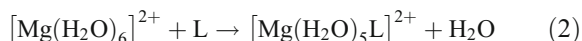
In Table 1 we list the interaction enthalpy values for the substitution of one water molecule by a ligand. Analysis of Table 1 reveals that essentially all the substitution energies are negative (with the exception of the strong electron withdrawing NO_2 group in the thiocarbonyl derivative), showing that the substitution of one water molecule by a ligand is an exothermic process, in agreement with previous studies [16, 27, 32–35]. The imino ligands have stronger
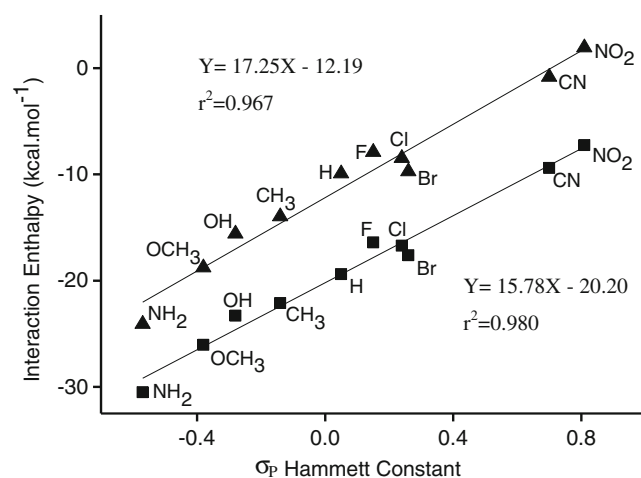
interaction with the Mg^{2+} cation than the thiocarbonyl ligands. The substitution energy with the imino ligands is 8.14 ± 0.89 kcal mol^{-1} more negative than with the thiocarbonyl ligands. This is the same trend found when we analyzed the geometric parameters, showing that the electrostatic term must be the major component of the interaction. The analysis of the interaction enthalpy in each set of ligands shows an interesting trend related to the nature of the *para*-substituted group. Figure 3 shows the correlation between the interaction enthalpy and the values of the σ_P Hammett constant of the *para*-substituents in each set of imino and thiocarbonyl ligands. A visual inspection of Fig. 3 shows that ligands with electron donor substituents have more negative interaction enthalpies than ligands with electron withdrawing groups. This electronic modulation on the interaction enthalpy exerted by the *para*-substituted group is due to the resonance effect that provides the final charge density on the S or N atom that interacts with the Mg^{2+} aquacenter. This behavior has been previously reported for the interaction of ligands with the chromium [24], lithium [25] and calcium [16, 32–35] cations.

In each set of ligands the amino *para*-substituted complex gives the most negative interaction enthalpy, whereas the nitro group gives the less exothermic enthalpy. The amino-nitro difference in the imino complexes is 22.87 kcal mol^{-1}, while in the thiocarbonyl derivatives it is 26.02 kcal mol^{-1}, showing that the substituent effect is stronger in the sulfur complexes. In Fig. 3 we also show the linear fitting parameters. They quantify the interaction enthalpy order given above and confirm that the substituent effect is stronger in the thiocarbonyl derivatives. The interaction enthalpy of both imino and thiocarbonyl complexes have high correlation with the σ_P Hammett parameter, as shown in Fig. 3. It is important to note that the d_1 and d_2 distances are highly correlated with the interaction enthalpy with correlation coefficients of $r^2 = 0.933$ and $r^2 = 0.980$ for the imino and thiocarbonyl derivatives, respectively.

The qualitative effect of each *para*-substituted group is well reproduced by the PM6-DH2 semi-empirical method for both the imino and thiocarbonyl complexes ($r^2 = 0.979$ and $r^2 = 0.987$ for the imino and thiocarbonyl compounds, respectively). However, a quantitative analysis shows that the semi-empirical interaction enthalpies are more negative than those obtained with the B3LYP/6-31+G(d) method, in accordance with previous studies [32–35, 56, 57]. The PM6-DH2 interaction enthalpies are 12.90 ± 1.03 kcal mol^{-1} and 15.49 ± 1.45 kcal mol^{-1} more negative than the DFT values for the imino and thiocarbonyl complexes, respectively. It is important to note that the same energy trends were obtained in the PM6-DH2 calculation, with the interaction energy being stronger for the imino compounds than for the thiocarbonyl compounds. The PM6-DH2 approach also reproduces the fact that derivatives with electron donor

Fig. 3 B3LYP/6-31+G(d) correlation between the interaction enthalpy and the Hammett σ_P constant for the pentaaqua Mg^{2+} complexes containing imino (*black square*) and thiocarbonyl (*black up-pointing triangle*) ligands

substituents have stronger interaction energy with the metal center than compounds with electron acceptor substituents.

In Table 1 we also list the interaction Gibbs free energy (ΔG^{298}) values for the imino and thiocarbonyl complexes. For almost all complexes the ΔG^{298} is negative, showing that the substitution of one water molecule for a ligand is a spontaneous process, with only the exception of the nitro thiocarbonyl derivative. The magnitude of the ΔG^{298} values follows the same trends as the enthalpy, with the ΔG^{298} for the imino complexes being 7.94 ± 1.15 kcalmol^{-1} more negative than those for the thiocarbonyl compounds. This parameter is also influenced by the nature of the substituent, with the differences between the amino and nitro derivatives being 23.28 kcalmol^{-1} for the imino and 25.79 kcalmol^{-1} for the thiocarbonyl complexes. This additional parameter also shows that the electronic modulation is stronger in the thiocarbonyl set than in the imino compounds.

As a typical bond with a high electrostatic component, the charges on the atoms that participate in the interaction are important to determine the strength of binding. In Table 1 we list the atomic charges on the N and S atoms that interact with the Mg^{2+} cation for isolated imino and thiocarbonyl ligands. The analysis shows that the charges on the nitrogen atoms of the imino group are 0.385 ± 0.036 e$^-$ more negative than those on the sulfur atom of the thiocarbonyl group. This is the same order found in the analysis of the geometrical parameters and shows that the imino ligands have the strongest electrostatic component of the interaction. The charge analysis in each set of ligands shows that the substituent group determines the atomic charge on the atom that interacts with the pentaaqua Mg^{2+} cation. Electron donor substituents lead to higher charge densities on the N or S atoms than electron withdrawing substituents. The differences between the amino and nitro derivatives are 0.248 e$^-$ and 0.100 e$^-$ for the imino and thiocarbonyl complexes, respectively.

The charge on the whole ligand after complexation was also analyzed. Net electronic charge on either the ligand or the $[Mg(H_2O)_5]^{2+}$ moiety is a consequence of electron transfer between the fragments and gives an indication of the covalent component of the interaction. Table 2 shows that charge on the ligand moiety after complexation is always positive, indicating charge transfer from the ligand to the $[Mg(H_2O)_5]^{2+}$ cation. The charges on the ligand moiety for the thiocarbonyl derivatives are more positive (by 0.153 ± 0.004 e$^-$) than those for the imino derivatives, showing that in the thiocarbonyl derivatives the covalent contribution to the total interaction energy is more relevant. Analysis in each set of ligands shows that in the amino derivatives charges on the ligand are more positive (by 0.049 e$^-$ and 0.046 e$^-$ for the imino and thiocarbonyl derivatives, respectively) than in the nitro substituted complexes. These charges also correlate with the interaction

Table 2 Total interaction energy (ΔE_{Int}), electrostatic (ΔE_{Elstat}), exchange (ΔE_{Exch}), polarization (ΔE_{Pol}), dispersion (ΔE_{Disp}) and Pauli repulsion (ΔE_{Pauli}) components, in kcalmol^{-1}, of the Mg^{2+}-ligand interaction

	ΔE_{Int}	ΔE_{Elstat}	ΔE_{Exch}	ΔE_{Pol}	ΔE_{Disp}	ΔE_{Pauli}
Imino ligands						
NH$_2$	−79.27	−66.73	−8.37	−38.98	−6.52	41.33
OCH$_3$	−72.94	−61.20	−8.02	−37.39	−6.36	40.03
OH	−70.13	−59.16	−7.91	−36.12	−6.26	39.32
CH$_3$	−67.90	−56.90	−7.77	−35.76	−6.21	38.74
H	−65.29	−54.45	−7.48	−35.46	−6.14	38.24
F	−61.75	−51.67	−7.46	−34.11	−6.03	37.52
Cl	−62.58	−51.89	−7.51	−34.85	−6.06	37.73
Br	−63.58	−52.69	−7.53	−35.28	−6.11	38.03
CN	−54.05	−43.44	−7.03	−33.72	−5.97	36.11
NO$_2$	−52.47	−42.04	−6.67	−33.24	−5.85	35.33
Thiocarbonyl ligands						
NH$_2$	−70.10	−53.54	−9.07	−41.85	−5.77	40.13
OCH$_3$	−63.35	−46.74	−8.58	−40.30	−5.7	37.97
OH	−60.87	−44.35	−8.31	−39.85	−5.61	37.25
CH$_3$	−56.61	−40.67	−8.03	−38.45	−5.51	36.05
H	−53.29	−37.26	−7.85	−38.26	−5.46	35.54
F	−49.34	−34.78	−7.64	−36.12	−5.35	34.55
Cl	−50.52	−35.02	−7.69	−37.31	−5.38	34.88
Br	−52.17	−36.33	−7.77	−38.04	−5.4	35.37
CN	−41.73	−26.14	−7.08	−36.06	−5.01	32.56
NO$_2$	−39.04	−24.22	−6.84	−34.83	−4.76	31.61

enthalpy, $r^2 = 0.939$ and $r^2 = 0.984$ for the imino and thiocarbonyl ligands, respectively. These same trends were found by Palusiak [24], Senapati [25] and Gal [26] when studying the interaction between metal divalent cations and monofunctional ligands.

Binding preference prediction The binding preference of the $[Mg(H_2O)_5]^{2+}$ cation for a ligand was evaluated through calculation of the absolute softness (S) of each ligand. The absolute softness values for the imino and thiocarbonyl ligands are listed in Table 1. Analysis of the absolute softness inherent to each functional group (imino or thiocarbonyl) shows that the thiocarbonyl ligands have the largest absolute softness, 0.760 ± 0.074 higher than that of the imino derivatives. As the sulfur atom has larger atomic radius and lower electronegativity than the nitrogen atom, its electronic cloud is more polarizable, resulting that the thiocarbonyl ligands are softer than the corresponding imino derivatives [15]. Based on the HSBA theory the $[Mg(H_2O)_5]^{2+}$ cation may be considered a hard specie, therefore a stronger interaction with the imino than with the thiocarbonyl derivatives may be expected. Additionally, due to the difference in absolute softness of

the two classes of ligands we could anticipate that the covalent contribution to the total interaction energy between the $[Mg(H_2O)_5]^{2+}$ cation and the ligands will be higher for the thiocarbonyl than for the corresponding imino derivatives. Analysis of the absolute softness in each set of functional group shows that the electronic nature of the substituent is an important factor to determine this property. Ligands with electron donor groups (NH_2, OCH_3, OH) have higher absolute softness than ligands with electron withdrawing groups (CN, NO_2). The amino-nitro absolute softness difference is 0.21 ± 0.067 for the imino compounds and 0.29 ± 0.099 for the thiocarbonyl derivatives. The electron donor groups increase the electron density on the S and N atoms increasing their softness, while the electron withdrawing groups decrease the electron density on those atoms, making the interacting center less polarizable (harder). This trend shows that ligands with electron donor groups must have a stronger covalent component in the interaction with the $[Mg(H_2O)_5]^{2+}$ cation than ligands with electron withdrawing groups. The larger atomic radius of the S atom compared with that of the N atom makes the variation of the absolute softness in the thiocarbonyl group higher than that in the imino set. This absolute softness order was found in previous studies [58–60]. A detailed analysis of the nature of the metal-ligand interaction is given bellow.

Energy decomposition analysis The EDA method [51] decomposes the metal-ligand interaction into five terms: the electrostatic, exchange, polarization, dispersion and Pauli repulsion components, derived from charge attraction, parallel spin densities, orbital overlapping, long range interactions and charge repulsion, respectively. The sum of these components defines the total interaction energy that, as the substitution enthalpy shown above, is a measure of the strength of the metal-ligand binding. In Table 2, we list the total interaction energies between the pentaaqua Mg^{2+} cation and the imino and
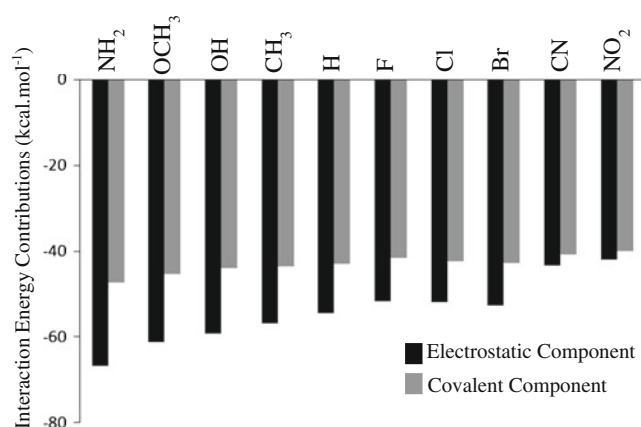

Fig. 4 Ionic and covalent components of the metal-ligand interaction for the imino complexes
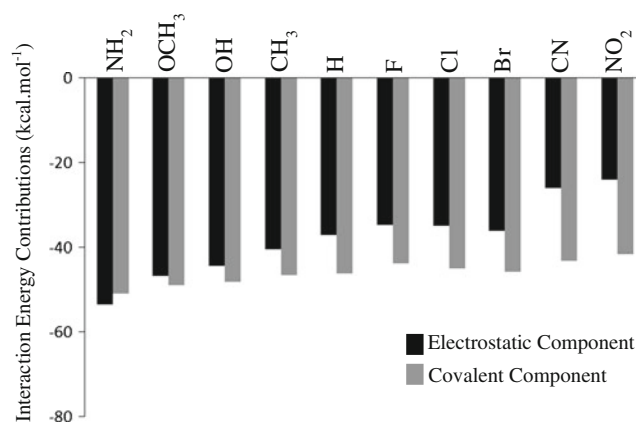

Fig. 5 Ionic and covalent components of the metal-ligand interaction for the thiocarbonyl complexes

thiocarbonyl ligands. The results indicate the same trends obtained in the substitution enthalpy, but with more negative values. The interaction between the Mg^{2+} cation with the imino ligands is 11.29 ± 1.47 kcal mol^{-1} stronger than with the thiocarbonyl derivatives. The electronic characteristic of the ligands also modifies the degree of the metal-ligand interaction. Complexes with electron donor substituents have more negative interaction energies than those with electron withdrawing groups. The difference between the amino and the nitro derivatives is 26.80 kcal mol^{-1} for the imino and 31.06 kcal mol^{-1} for the thiocarbonyl complexes. The amino-nitro difference is larger for the thiocarbonyl set than for the imino, by about 5 kcal mol^{-1}, due to the softer electronic cloud of the sulfur atom that allows easier electron polarization and delocalization promoted by the substituted group. Interesting trends were obtained in the analysis of the components of the total interaction energy. In Figs. 4 and 5 we show the dependence of the electrostatic and covalent (exchange+polarization energies) components as a function of the substituent for the imino and thiocarbonyl ligands, respectively. A visual inspection shows that the electronic nature of the substituent modulates more strongly the electrostatic term than the covalent component of the metal-ligand interaction. In both sets, the amino derivatives have the strongest ionic character, which gradually decreases as we move in the direction of the strongest withdrawing substituent (NO_2). In the imino set, the interaction is predominantly electrostatic, with exception of the strong electron withdrawing CN and NO_2 substituents, where the electrostatic and covalent components have essentially the same value. The thiocarbonyl set shows the opposite behavior. The interaction is almost 50 % of each component (electrostatic and covalent) in the strong electron donor substituted complexes, while it is predominantly covalent in the complexes with electron withdrawing groups. The different nature of each interaction resides in the electronic features of the atom that interacts with the Mg^{2+} cation. The nitrogen atom has smaller atomic radius and is more electronegative than the

sulfur atom, thus concentrating more negative charge, strengthening the electrostatic interaction. This is the same trend observed in the analysis using the HSAB model. The larger and more polarizable electronic cloud of the sulfur atom favors electron donation to the metal center, increasing the overlap of the orbitals and, consequently, the covalent component [15]. Similar trends were previously reported by Baskaran for the interaction between monofunctional ligands and copper complexes [29].

In Table 2, we also list the values of the five components of the metal-ligand interaction. The electrostatic component of the imino complexes is stronger than those of the thiocarbonyl derivatives, as previously seen in the analysis of Fig. 3. The imino electrostatic energies are 16.11 ± 1.48 kcalmol^{-1} more negative than those for the thiocarbonyl compounds. Complexes with electron donor substituents have stronger electrostatic contribution than complexes with electron withdrawing substituents, 24.69 kcalmol^{-1} and 29.32 kcalmol^{-1} for the imino and thiocarbonyl set, respectively. This is the component most strongly affected by the electronic nature of the substituent [51]. Table 2 also shows the individual values of the exchange and polarization contributions to the covalent interaction. The polarization contribution is at least six times larger than the exchange value, being the major one in both sets. The polarization component for the thiocarbonyl complexes are slightly more negative, 2.62 ± 0.57 kcalmol^{-1}, than for the imino derivatives.

Analysis of the covalent component in each set of ligands shows that the amino-nitro difference is at least four times lower than the corresponding value of the electrostatic component. The amino-nitro covalent component difference is 5.74 kcalmol^{-1} for the imino and 7.02 kcalmol^{-1} for the thiocarbonyl complexes. The electronic nature of the substituent modulates the electron density, but with no significant effect on the orbital interaction, thus minimizing the variation of the polarization contribution. The exchange component in both sets of complexes is almost constant, with variation of less than 1 kcalmol^{-1} and is not directly related with the electronic nature of the substituent [51]. The dispersion component of the metal-ligand interaction is also essentially constant along both sets varying by less than 2 kcalmol^{-1}. This component is more affected in the system containing long range interactions like π-π stacking [53]. In Table 2 we also list the values of the Pauli repulsion term of the interaction. It shows that the repulsion in the imino ligands is 2.65 ± 0.74 kcalmol^{-1} larger than in the thiocarbonyl derivatives. The Pauli repulsion term is strongly correlated ($r^2 = 0.976$) with the distance between the atoms that form the interaction (d_1). As the metal-ligand distance is higher in the thiocarbonyl derivatives they have lower Pauli repulsion. The variation of the Pauli repulsion in each set of ligands follows this same trend. In the imino set the amino-nitro difference is 6.00 kcal mol^{-1} and in the thiocarbonyl set it is 8.52 kcalmol^{-1}.

Conclusions

The ability of imino and thiocarbonyl ligands to complex the $[Mg(H_2O)_5]^{2+}$ cation was evaluated in terms of geometric (d_1 and d_2 distances), energetic (HSAB index, interaction enthalpy and EDA analysis) and electronic (charges on the nitrogen and sulfur atoms and on the ligand) parameters. Twenty *para*-substituted ligands with a wide range of electronic effects were analyzed and their influence on the strength of the metal-ligand interaction was determined. The interaction enthalpy analysis shows that imino ligands bind more strongly to the pentaaqua Mg^{2+} cation than the thiocarbonyl derivatives. This is mainly due to the electronic nature of the atoms that interact with the metal center. The nitrogen atom is smaller, with a higher electronegativity that strengths the interaction with the alkaline earth Mg^{2+} cation, with more charge attraction and smaller interaction distances. Electron donating substituents strengthen the ligand-cation interaction, leading to a more exothermic interaction enthalpy, while electron withdrawing substituents have the opposite effect. The electron donating groups strengthen the cation-ligand interaction by increasing both its electrostatic and covalent components. The HSAB indexes also show that the imino ligands have a higher binding preference toward the Mg^{2+} cation than the thiocarbonyl ligands. The EDA analysis shows that the electronic nature of the substituent modulates more strongly the electrostatic, polarization and repulsion terms of the interaction. Using the EDA approach, we were able to show that the differences in the abilities of the ligands to complex the cation are mainly due to differences in the electrostatic component of the interaction enthalpy. The exchange and dispersion components are almost constant for both the imino and thiocarbonyl derivatives with variations of less than 2 kcal mol^{-1}. For the imino complexes the electrostatic term is the major one, while for the thiocarbonyl complexes the covalent component is stronger than the ionic component.

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